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CLINICAL STUDIES

Left Ventricular Remodeling in the Year After First Anterior Myocardial Infarction: A Quantitative Analysis of Contractile Segment Lengths and Ventricular Shape

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Infarct expansion after myocardial infarction results in early ventricular enlargement and distortion of ventricular geometry. To characterize the components of late volume enlargement, biplane left ventriculography was performed in 52 patients 3 weeks and 1 year after a first anterior myocardial infarction. Biplane diastolic circumference and contractile and noncontractile segment lengths were measured. Global geometry was evaluated by using a sphericity index (angiographic volume of the ventricle divided by the volume of a sphere with the same circumference). Regional geometry was assessed by measurement of endocardial curvature, an important determinant of wall tension.

End-diastolic volume was enlarged at baseline and increased at 1 year (230 ± 42 to 244 ± 55 ml, p = 0.01) as a result of increases in contractile segment length (34 ± 5 to 37 ± 5 cm, p < 0.001) and sphericity index (0.74 ± 0.07 to 0.76 ± 0.08, p < 0.001), whereas the noncontractile segment length decreased (15 ± 6 to 12 ± 6 cm, p < 0.005). Curvature analysis revealed a flattening of presumably high tension concavity at the anterobasal (−6.0 ± 4.0 to −4.5 ± 3.7, p < 0.01) and inferior (−4.5 ± 2.6 to −3.6 ± 2.1, p < 0.005) margins of the infarct and less bulging of the anterior wall (9.4 ± 2.5 to 8.2 ± 2.3, p < 0.001). Patients selected for late enlargement (diastolic volume increase >20 ml, n = 19) had an increase in sphericity (0.75 ± 0.05 to 0.80 ± 0.08, p < 0.005) and in diastolic circumference (54 ± 3 to 56 ± 4 cm, p < 0.001) secondary to elongation of the contractile segment (32 ± 4 to 36 ± 4 cm, p = 0.001) at 1 year.

Thus, late ventricular enlargement after anterior infarction results from an increase in contractile segment length and a change in ventricular geometry and is not a result of progressive infarct expansion. In the group of patients at high risk for late ventricular enlargement because of persistent occlusion of the infarct-related vessel, captopril therapy attenuated late volume enlargement by preventing these changes in contractile segment length and chamber geometry.

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Myocardial infarct expansion, the acute process of lengthening and thinning of the infarcted zone, results in early ventricular chamber enlargement with regional as well as global distortion of the shape of the left ventricle (1–4). This expansion of the noncontractile myocardial segment, an early consequence of slippage and elongation of necrotic myocyte bundles (5), may be associated with late structural changes that continue during the healing phase. Late increases in ventricular volume have been demonstrated during the long-term phase of recovery from myocardial infarction (6–11); however, the precise regional remodeling that leads to late left ventricular dilation in this patient cohort has not been described.

The purpose of the present study was to examine the characteristics of late ventricular enlargement and to determine the role of changes in the length of contractile and noncontractile myocardial segments in the process of left ventricular remodeling after myocardial infarction. In addition, we sought to define the contribution of regional and global left ventricular shape to this process of late ventricular remodeling.

Methods

Study patients. This analysis of the components of ventricular enlargement utilized the quantitative left ventriculograms from a randomized, double-blind, placebo-controlled trial designed to evaluate the effects of captopril therapy on late ventricular chamber enlargement in the year after a first anterior Q wave myocardial infarction (10). Other inclusion criteria for participation in the study were documented

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infarction ≤30 days before randomization, radionuclide left ventricular ejection fraction of ≤45%, age between 21 and 75 years and freedom from symptoms of ischemia or congestive heart failure. The study protocol was approved by the Human Subjects Committee of Brigham and Women's Hospital and each patient gave informed consent to participate in the study. Of the 59 patients who participated in the study, 52 had baseline and 1-year ventriculograms of adequate technical quality for the quantitative analyses required for this report. Clinical characteristics of the patients and reasons for failure to complete the study (seven patients) have been previously reported (10).

Cardiac catheterization protocol. Both the baseline and 1-year studies included left and right heart catheterization and determination of cardiac output by the Fick method. Biplane left ventriculography was performed in the 30° right anterior oblique and 60° left anterior oblique projections at a rate of 30 frames/s per view. The baseline study included coronary angiography with multiple views.

Drug therapy. After baseline catheterization (12 to 31 days after myocardial infarction), all patients were randomly assigned to either captopril or placebo in addition to conventional therapy. One year (364 ± 11 days) after baseline catheterization, repeat ventriculography was performed by the same investigators with careful attention to appropriate corrections for radiographic magnification. Study medication was discontinued 1 day before follow-up catheterization.

Data analysis. Ventricular silhouettes were traced onto transparency film and then digitized at a resolution of 10 points/mm by using a digitizing tablet interfaced to a personal computer. Corrections for magnification and pincushion distortion were made based on a library of calibrated grid information maintained in a computer data base. Left ventricular volumes were determined by the area/length method (ellipsoid model) by using a regression equation developed at this institution (12).

Wall motion and length of contractile segment. Wall motion was analyzed at 100 chords (Fig. 1, top panel) by a modification of the centerline method (13) in which, rather than a shortening fraction, absolute magnification-corrected wall displacement was standardized (Z score) for analysis. Further, the centerline algorithm for patients with left anterior descending coronary artery lesions was used in every case regardless of coronary anatomy. This ensured that in each study maximal hypokinesia was measured in the anterior region (chords 10 to 66) and maximal hyperkinesia in the inferior region (chords 67 to 80). The percent of each silhouette that was either akinetic (uncorrected wall motion 0 ± 1 mm) or dyskinetic (more negative than −1 mm) was calculated and multiplied by the magnification-corrected diastolic circumference to obtain the absolute noncontractile segment length in centimeters. The length of the contractile segment was similarly obtained by using the sum of the remaining chords. The aortic outflow tract was excluded from either of these determinations of contractile status but

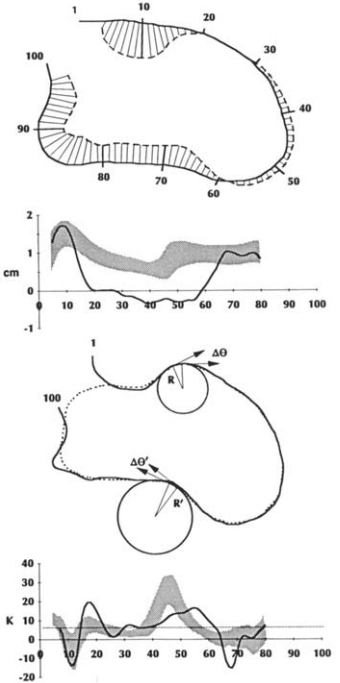

Figure 1. Centerline wall motion and curvature analysis. The **top panel** presents an example of centerline wall motion analysis in a patient with an anterior myocardial infarction. The **bottom panel** illustrates the calculation of curvature using the systolic outline of the same patient. The **broken line** represents the smoothed silhouette on which curvature calculations are performed, as detailed in the text. Curvature (K) is a measure of the change in the angle of the tangent vector with respect to path length along the endocardial silhouette. For example, the first radius (R), which corresponds to point 17, occurs in a region of rapid change in the tangent angle ($\Delta\theta$) and represents an area of relatively high curvature ($K = 1/R$) or short radius of curvature. Thus, the "best fit" or "unit" circle for that area is relatively small. For the second radius (R') at point 67, the change in the tangent angle is less marked so that the unit circle is larger, making the magnitude of curvature smaller. Also, the change in tangent angle is to the left (concave) of R' so that the value for curvature is negative. Note that at the borders of the infarct, the areas of negative curvature are produced by the juxtaposition of functioning and nonfunctioning tissue (chords 10 to 14 and 65 to 70), as seen on the wall motion plot. The **shaded area** in each plot is the normal mean value ± 1 SD.

was included in the total circumference. Values obtained from right and left anterior oblique views were summed to give the biplane circumference and its component contractile and noncontractile endocardial segment lengths.

Sphericity index. To evaluate changes in global left ventricular shape, a circumference-based modification of a previously described sphericity index (14) was defined that expresses the measured diastolic or systolic volume of the ventricle (ellipsoid model) as a fraction of the volume of a hypothetical spherical left ventricle with the same biplane diastolic or systolic endocardial circumference, respectively. This method of evaluating the global shape of the ventricle allows for estimation of the relative contribution of a change in shape versus an increase in endocardial circumference to an increase in ventricular chamber volume. For example, if one calculates the theoretic volume (V_{th}) of a given ventricle by using the measured endocardial circumference but assuming a normal sphericity index, then the difference between the measured volume of the ventricle and V_{th} represents the excess volume due to sphericity, and the difference between V_{th} and the volume of a normal ventricle would be the excess volume due to circumference.

Regional shape. This was assessed by measuring the local major axis (right anterior oblique) curvature (Fig. 1, bottom panel) (15). Before calculation of curvature (K), which is the reciprocal of radius (R) of curvature ($K = 1/R$), each silhouette was converted to polar coordinates (256 points) and expressed as a Fourier series by using a fast Fourier transform (16). Before reverse transformation, the Fourier series was smoothed with a Hanning filter that drops to 0 at the 20th harmonic, thus eliminating the high frequency artifact resulting from hand-tracing and digitization. The smoothed silhouette was converted back to Cartesian coordinates and curvature was calculated at each point based on a 5-point, second-order polynomial fit. From these 256 values for curvature, 100 values were extracted by quadratic interpolation at points corresponding to the centerline wall motion chord intersections (Fig. 1). This reference system allows for direct comparisons between local shape and wall motion. Curvature, in cm^{-1}, was normalized to ventricular size and made unitless by multiplying each value by the circumference ($2\pi R$) of the silhouette (diastolic or systolic) being analyzed. Because of this normalization procedure, a spherical ventricle (sphericity index = 1) would have a corrected curvature value of $(2\pi R)(1/R) = 2\pi$ at every point along its perimeter regardless of its size. Convexity is denoted by positive curvature, whereas a negative value indicates concavity of the endocardial silhouette.

Endocardial curvature. The important features of endocardial curvature were summarized by searching each of four anatomic and functional left ventricular regions and finding the contiguous 50% of the points within each region that are least abnormal in noninfarcted regions or most abnormal in infarcted regions. Thus, in the anterobasal region (points 5 to 17) a curvature minimum is found (accentuation of the normal finding); in the infarcted anterior region (points 13 to 34) a maximum is found (most abnormal); at the apex (points 35 to 65) the maximal value is found (least abnormal) and in the inferior region (points 60 to 80) a minimum is found (accentuation of normal negative curvature). This approach eliminates the hazards of using fixed reference points to describe variable anatomic landmarks. For example, the apex may shift to the right or left but maintain its normal peak curvature after infarction or during recovery or as a variant of normal. Such a shift will have no effect on this system of dynamic localization of peak apical curvature.

Normal values. Noninfarcted reference values for all hemodynamic data and for right anterior oblique curvature were obtained from the left ventriculograms of 76 patients without coronary artery disease or a history of myocardial infarction. Normal values for biplane ventriculographic variables were obtained from the 37 of these patients who had biplane studies.

Statistical analysis. Changes (baseline to 1 year) in hemodynamic variables and derived ventriculographic variables (volume, contractile and noncontractile segment lengths, regional wall motion, sphericity and curvature) in the entire study group (n = 52) regardless of drug therapy were analyzed with a paired *t* test. Because late ventricular enlargement is a heterogeneous process that does not equally affect all patients, we analyzed intra- and interobserver variability for duplicate determinations of left ventricular volumes from the baseline angiograms and thereby defined significant enlargement as an increase in end-diastolic volume >20 ml. The subgroup of 19 patients with marked late ventricular dilation and the subgroup of 33 patients with no significant increase or a decrease in end-diastolic volume were then analyzed to determine the components of this late change in ventricular volume, again without regard to drug therapy.

Previous observations (10) have revealed that captopril therapy was most effective in attenuating late ventricular enlargement in those patients with persistent occlusion of the infarct-related vessel. Therefore, the effects of therapy on the components of ventricular remodeling were analyzed in patients with persistent occlusion of the left anterior descending coronary artery who were randomized to placebo (n = 15) or to captopril (n = 21) therapy. Differences were considered significant if a two-tailed test gave a p value <0.05. Data are presented as mean values ± SD.

Results

Baseline catheterization (Table 1). At the time of baseline catheterization (11 to 31 days after myocardial infarction), all patients were found to have disease of the proximal (n = 51) or mid (n = 1) left anterior descending coronary artery, which was a large vessel that supplied the left ventricular apex in all patients. Persistent total occlusion of the artery was apparent in 36 (67%) of the 52 patients. On initial catheterization, mildly elevated left ventricular end-diastolic

Table 1. Paired Ventriculographic Data for 52 Patients With Anterior Myocardial Infarction

	3 Weeks	1 Year	p Value
End-diastolic volume (ml) (142 ± 31)	230 ± 42	244 ± 55	0.010
End-systolic volume (ml) (40 ± 14)	136 ± 40	142 ± 54	—
Ejection fraction (0.72 ± 0.08)	0.42 ± 0.10	0.43 ± 0.11	—
Diastolic sphericity index (0.66 ± 0.08)	0.74 ± 0.07	0.76 ± 0.08	0.001
Systolic sphericity index (0.49 ± 0.11)	0.62 ± 0.10	0.65 ± 0.10	0.001
Diastolic circumference (cm) (47 ± 4)	53 ± 3	54 ± 4	—
Systolic circumference (cm) (35 ± 4)	48 ± 4	47 ± 5	—
Contractile segment (cm) (43 ± 4)	34 ± 5	37 ± 5	<0.001
Noncontractile segment (cm) (0 ± 0)	15 ± 6	12 ± 6	0.003
Akinetic	8 ± 5	6 ± 4	<0.001
Dyskinetic	6 ± 4	7 ± 4	—

Values in parentheses indicate normal mean values ± SD; p values = paired *t* test, 3 weeks versus 1 year.

pressure (20 ± 6 mm Hg) was associated with marked elevation of both end-diastolic and end-systolic volume compared with values in patients without infarction, consistent with substantial early left ventricular enlargement. Baseline diastolic circumference and sphericity index were both increased in the study group, indicating that early ventricular enlargement resulted from a combination of increased biplane endocardial circumference and increased sphericity of the ventricle. Assuming that ventricular volume and sphericity were comparable to normal before infarction, then of the 88-ml early postinfarction end-diastolic chamber enlargement, 66 ± 38 ml can be attributed to an elongated diastolic circumference and 22 ± 23 ml to increased sphericity. Similarly, of the 96-ml elevation in baseline end-systolic volume, 69 ± 27 ml can be attributed to increased circumference and 27 ± 23 ml to increased sphericity.

Catheterization at 1 year (Table 1). In the year after infarction the overall group exhibited a further increase in end-diastolic volume despite a reduction in end-diastolic pressure (from 20 ± 6 to 18 ± 7 mm Hg, $p < 0.02$). This increase in diastolic volume was the result of further distortion of the shape of the ventricle to a more spheric configuration, since the biplane circumference did not change significantly. The increase in end-diastolic volume was accompanied by a stable end-systolic volume, leading to an increase in stroke volume and preservation of the Fick cardiac output (5.8 ± 1.7 vs. 5.6 ± 1.4 ml/min, p = NS) despite a reduction in heart rate (from 72 ± 13 to 67 ± 11 min^{-1}, $p < 0.01$).

Wall motion analysis. In the overall group, 15 ± 6 cm (27 ± 11%) of the 53 ± 3-cm biplane end-diastolic circumference was either akinetic or dyskinetic at baseline. At the 1 year follow-up, despite no further change in the total circumference, there was a 2.7 ± 4.9-cm elongation of the contractile endocardial segment ($p < 0.001$) and a concomitant 2.3 ± 5.3-cm decrease in the length of the noncontractile segment ($p < 0.005$). Division of the noncontractile segment into akinetic and dyskinetic components revealed that the decrease was confined to the akinetic segment, which was 2.4 ± 4.6 cm shorter at 1 year ($p < 0.001$), whereas the dyskinetic segment remained unchanged.

As anticipated, baseline centerline wall motion in the anterior (infarct) zone was severely depressed, whereas wall motion in the noninfarcted inferior zone (the most vigorously contracting contiguous 50% of the chords in the inferior region) was not hyperkinetic as might be expected, but was mildly depressed. Catheterization at 1 year revealed a slightly improved score in the anterior zone (from −3.4 ± 0.6 to −3.2 ± 0.8 SD/chord, $p < 0.02$) with mild deterioration in the inferior region (from −0.2 ± 1.0 to −0.6 ± 1.0 SD/chord, $p < 0.05$).

Left ventricular geometry (Fig. 2). In conjunction with abnormal left ventricular regional wall motion and global shape, we found severe abnormalities in endocardial curvature at baseline in the patients with anterior Q-wave infarction compared with findings in the patients without infarction (Fig. 2). Specifically, at end-systole (Fig. 2, third panel), when changes induced by heterogeneous ventricular contraction are most marked, adjacent to the negative curvature (concavity) associated with anterobasal contraction (points 5 to 17), there was excessive curvature (bulging) of the anterior wall (points 13 to 34). There was diminished curvature (blunting) and rightward or clockwise shifting of the apex (points 35 to 65) and excessively negative curvature (concavity) of the inferior region (points 60 to 80). When the curvature change from diastole to systole was analyzed (Fig. 2, bottom panel), the normal systolic increase in curvature in the apical region was totally absent.

Regional systolic curvature summaries in the patient group at baseline and at 1 year confirm the findings presented in the baseline curvature plots as described earlier. At 1 year, concavity became less prominent in the anterobasal (−6.0 ± 4.0 vs. −4.5 ± 3.7, $p < 0.01$) and inferior (−4.5 ± 2.0 vs. −3.6 ± 2.1, $p < 0.005$) regions, bulging in the anterior wall decreased (9.4 ± 2.5 vs. 8.2 ± 2.3, $p < 0.001$) and blunting of the apex did not change (14.0 ± 1.4 vs. 14.1 ± 1.4, p = NS). Each of these regional changes approaches the spherical value of 2π, which is consistent with the observed increase in the global sphericity index (Table 1).

Patients with chamber enlargement (Table 2). Patients with and without chamber enlargement did not differ in the use of digoxin, beta-adrenergic blocking agents, calcium channel blocking agents, long-acting nitrates, diuretic agents, heparin, coumadin or antiarrythmic agents. There was also no difference in the presence of significant (>70%) stenosis of the left circumflex or right coronary artery, or both.

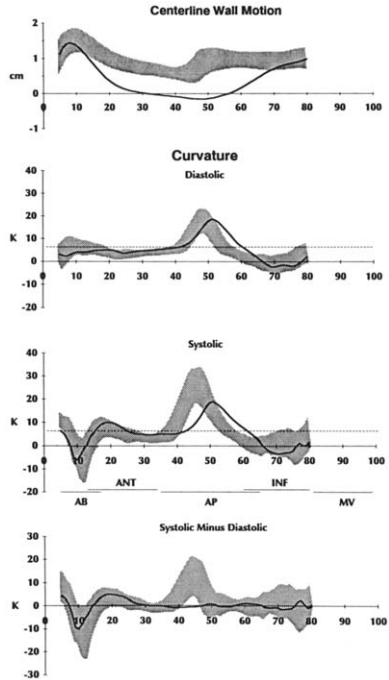

Figure 2. Baseline regional wall motion and curvature (K) in 52 patients who had anterior myocardial infarction and in 76 normal patients. The **top panel** illustrates absolute centerline wall motion in cm and the **second and third panels** are normalized diastolic and systolic curvature plots, respectively. The **fourth panel** represents the change in curvature from diastole to systole. The **shaded area** in each panel is the normal mean value ± 1 SD. The **broken line** in the diastolic and systolic curvature plots indicates the spheric value of $2\pi = 6.28$. Chord ranges marked by **solid lines** at the bottom of the systolic curvature plot represent the search regions for curvature averages presented in the text. Values before chord 5 (the aortic outflow tract) and beyond chord 80 (the mitral valve plane) are excluded for clarity. See text for details. AB = anterobasal; ANT = anterior; AP = apical; INF = inferior; MV = mitral valve.

In the 19 patients selected for late diastolic chamber enlargement, the 50 ± 27-ml increase above the already elevated baseline occurred with no change in distending pressure (22 ± 8 vs. 20 ± 6 mm Hg) (Table 2). This late increase in volume was due to a combination of increased circumference (equivalent to 31 ± 28 ml) and increased sphericity (equivalent to 19 ± 18 ml). Associated with this diastolic enlargement was a 33 ± 38-ml ($p = 0.001$) increase in end-systolic volume, of which 23 ± 20 ml could be attributed to an increase in sphericity and 10 ± 24 ml to an increase in circumference. Despite these substantial increases in ventricular volumes, there was no change in ejection fraction at 1 year.

The 2.5 ± 2.2-cm increase in biplane end-diastolic circumference ($p < 0.001$) was a result of a 4.0 ± 4.4-cm elongation of the contractile segment ($p = 0.001$) and a concomitant 1.5 ± 5.0-cm shortening of the noncontractile segment (p = NS). In this group of patients with volume enlargement, centerline wall motion was severely depressed in the anterior region (−3.7 ± 0.6 SD/chord) and mildly depressed in the inferior region (−0.5 ± 1.1 SD/chord) at baseline and did not change significantly over time. Analysis of local shape revealed marked accentuation of the normal concavity in the anterobasal region (−7.8 ± 3.2). As in the overall group, there was bulging of the anterior wall (10.1 ± 2.6), blunting of the apex (13.9 ± 1.6) and excessive concavity of the inferior wall (−4.7 ± 1.9). At follow-up evaluation, the same pattern of decreased concavity in the anterobasal (up to −5.4 ± 2.9, $p < 0.005$) and inferior (−3.4 ± 2.3, $p < 0.01$) regions and less bulging in the anterior region (9.0 ± 2.6, $p < 0.02$) was observed (Fig. 3).

Patients without volume enlargement (Table 2). In the remaining 33 patients with no significant increase in end-diastolic volume, both diastolic and systolic volume and end-diastolic pressure (19 ± 5 vs. 17 ± 8 mm Hg, $p = 0.02$) decreased at 1 year. Associated with this late decrease in volume was a 0.9 ± 1.6-cm decrease in biplane diastolic circumference ($p < 0.005$)—a result of a 2.8 ± 5.4-cm shortening of the noncontractile segment ($p < 0.01$) that exceeded the 2.0 ± 5.1-cm elongation of the contractile segment ($p < 0.05$). In this group, centerline wall motion was markedly depressed at baseline in the anterior region (−3.3 ± 0.6 SD/chord) and normal in the inferior region (0.0 ± 1.0 SD/chord), with a modest deterioration in the inferior region at follow-up (up to −0.5 ± 1.0 SD/chord, $p < 0.05$).

There were minimal changes in local and global ventricular shape variables over time in these patients. Diastolic and systolic sphericity indexes were not significantly different at 1-year follow-up. In contrast to findings in the group with volume enlargement, concavity in the anterobasal region (−4.9 ± 4.0) was normal at baseline and did not change significantly at 1 year. As in the group with volume enlargement, bulging of the anterior wall was less severe at 1 year (9.0 ± 2.4 vs. 7.8 ± 2, $p < 0.01$). Blunting of the apex (14.1 ± 1.4) and excessive concavity of the inferior wall (−4.4 ± 2.1) were present at baseline and remained stable at 1 year follow-up.

Persistent occlusion of the infarct-related vessel: effects of therapy (Table 3). *Placebo treatment.* In the 15 patients with persistent occlusion of the left anterior descending coronary artery randomized to treatment with placebo, there was further diastolic chamber enlargement (25 ± 43 ml, p <

Table 2. Paired Ventriculographic Data According to Change in End-Diastolic Volume (EDV) at 1 Year in 52 Patients With Anterior Myocardial Infarction

	Change in EDV <20 ml (n = 33)			Change in EDV ≥20 ml (n = 19)		
	3 Weeks	1 Year	p Value	3 Weeks	1 Year	p Value
End-diastolic volume (ml) (142 ± 31)	227 ± 40	219 ± 37	0.021	236 ± 45	287 ± 54	<0.001
End-systolic volume (ml) (40 ± 14)	129 ± 37	118 ± 35	0.018	150 ± 43	182 ± 57	0.001
Ejection fraction (0.72 ± 0.08)	0.44 ± 0.09	0.47 ± 0.10	0.046	0.37 ± 0.10	0.38 ± 0.10	—
Diastolic sphericity index (0.66 ± 0.08)	0.73 ± 0.08	0.74 ± 0.08	—	0.75 ± 0.05	0.80 ± 0.08	0.004
Systolic sphericity index (0.49 ± 0.11)	0.61 ± 0.10	0.62 ± 0.09	—	0.63 ± 0.09	0.71 ± 0.10	<0.001
Diastolic circumference (cm) (47 ± 4)	53 ± 3	53 ± 3	0.003	54 ± 3	56 ± 4	<0.001
Systolic circumference (cm) (35 ± 4)	47 ± 4	45 ± 4	0.001	49 ± 4	50 ± 5	—
Contractile segment (cm) (43 ± 4)	36 ± 5	38 ± 5	0.031	32 ± 4	36 ± 4	0.001
Noncontractile segment (cm) (0 ± 0)	13 ± 6	11 ± 6	0.096	17 ± 6	16 ± 6	—
Akinetic	7 ± 4	5 ± 4	0.017	10 ± 5	7 ± 4	0.012
Dyskinetic	6 ± 4	5 ± 4	—	7 ± 4	9 ± 5	—

Values in parentheses indicate normal mean values ± SD; p values = paired *t* test, 3 weeks versus 1 year.

0.05), with no change in the end-diastolic pressure (21 ± 5 vs. 21 ± 8 mm Hg). This late increase in diastolic volume was a result of increased sphericity with no change in circumference. Again, the length of the noncontractile segment decreased substantially by 4.3 ± 3.6 cm ($p < 0.001$) despite the increase in volume. This decrease was accompanied by a 5.3 ± 3.2-cm increase in the length of the contractile segment ($p < 0.001$). Centerline wall motion was severely depressed in the anterior region (−3.6 ± 0.5 SD/chord) and mildly depressed in the inferior region (−0.3 ± 1.0 SD/chord) at baseline and did not change over time. There was marked accentuation of the normal concavity in the anterobasal region (−7.5 ± 3.9) and bulging of the anterior wall (9.7 ± 2.8), both of which moved toward a more spheric configuration at 1 year (to −4.9 ± 3.3 and 8.4 ± 1.9, respectively; $p < 0.01$ for both). Baseline blunting of the apex (13.7 ± 1.3) and excessive concavity of the inferior wall (−3.8 ± 1.6) did not change significantly at 1 year.

Figure 3. Late ventricular enlargement in a patient with anterior myocardial infarction, illustrating the early and late changes in ventricular volume and geometry that may occur after anterior infarction. Note the marked increase in volume as a result of increased circumference and sphericity. The late change in circumference is due to lengthening of contractile tissue rather than to further expansion of the infarcted, noncontractile segment. The increase in sphericity results from a rounding out of the sharp abnormalities in contour at the margins of the infarct. Circ = circumference (cm); CS = contractile segment (cm); DSI = diastolic sphericity index; EDV = end-diastolic volume (ml); ESV = end-systolic volume (ml); NCS = noncontractile segment (cm); SSI = systolic sphericity index.

Captopril therapy. In contrast, the 21 patients with persistent occlusion of the left anterior descending coronary artery randomized to captopril therapy had no further diastolic chamber enlargement (Table 3). Left ventricular end-diastolic pressure decreased significantly at 1 year from 22 ± 7 to 17 ± 8 mm Hg ($p < 0.005$). The stable end-diastolic volume was accompanied by stable contractile and noncontractile segment lengths and global shape. Centerline wall motion was severely depressed in the anterior region (−3.6 ± 0.6 SD/chord) and normal in the inferior region (0.0 ± 1.0 SD/chord) at baseline, with no change at 1 year. Local shape changes consisted of flattening of the bulging anterior wall (from 9.4 ± 2.5 to 8.2 ± 2.2, $p < 0.05$) and decreased concavity in the inferior region (from −5.3 ± 1.9 to −4.4 ± 1.8, $p < 0.05$), with no significant change in the anterobasal (−5.6 ± 3.6 to −4.7 ± 4.1) and apical (13.8 ± 1.1 to 14.0 ± 0.9) regions.

Discussion

Volume enlargement. Previous observations have clearly established that marked early left ventricular enlargement may be seen after myocardial infarction. In the present group of patients with a large anterior Q wave infarction (27% akinesia plus dyskinesia at baseline), this substantial early increase in volume was present when compared with values in patients without infarction and presumably occurred between the time of myocardial infarction and base-

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Table 3. Paired Ventriculographic Data in 36 Patients With Persistent Occlusion of the Infarct-Related Vessel: Captopril Therapy Versus Placebo

	Placebo (n = 15)			Captopril Therapy (n = 21)		
	3 Weeks	1 Year	p Value	3 Weeks	1 Year	p Value
End-diastolic volume (ml) (142 ± 31)	242 ± 35	268 ± 64	0.041	231 ± 48	241 ± 52	—
End-systolic volume (ml) (40 ± 14)	154 ± 39	166 ± 67	—	138 ± 37	140 ± 43	—
Ejection fraction (%) (0.72 ± 0.08)	0.37 ± 0.08	0.40 ± 0.12	—	0.41 ± 0.10	0.43 ± 0.15	—
Diastolic sphericity index (0.66 ± 0.08)	0.75 ± 0.05	0.79 ± 0.06	0.018	0.75 ± 0.07	0.76 ± 0.09	
Systolic sphericity index (0.49 ± 0.11)	0.65 ± 0.07	0.70 ± 0.09	0.008	0.62 ± 0.07	0.64 ± 0.09	—
Diastolic circumference (cm) (47 ± 4)	54 ± 3	55 ± 4	—	53 ± 4	54 ± 4	—
Systolic circumference (cm) (35 ± 4)	49 ± 3	48 ± 5	—	48 ± 4	47 ± 5	—
Contractile segment (cm) (43 ± 4)	33 ± 4	38 ± 4	<0.001	33 ± 4	35 ± 4	—
Noncontractile segment (cm) (0 ± 0)	17 ± 5	13 ± 6	<0.001	16 ± 5	14 ± 7	—
Akinetic	9 ± 5	6 ± 4	0.005	8 ± 4	7 ± 4	—
Dyskinetic	8 ± 4	7 ± 4	—	8 ± 4	8 ± 5	—

*Values in parentheses indicate normal mean values ± SD; p values = paired *t* test, 3 weeks versus 1 year.

line (3 weeks) catheterization. This early volume enlargement was the result of both increased endocardial circumference and a more spheric configuration of the ventricle. In the ensuing year, additional chamber enlargement occurred. This late ventricular enlargement was associated with significant lengthening of the contractile segment and with increasing sphericity of the ventricle despite a reduction in filling pressure, which alone would tend to decrease both the length of the contractile segment and the sphericity of the ventricle (17). The noncontractile segment length decreased during this chronic phase, suggesting that to the extent that akinesia plus dyskinesia estimates anatomic infarct size, infarct expansion did not contribute to late ventricular enlargement in this patient group. Even in the subgroup selected for significant late volume enlargement, lengthening of the noncontractile segment was not observed. In contrast, in the group with volume enlargement, there was substantial lengthening of the contractile segment at a constant left ventricular filling pressure, suggesting true hypertrophy rather than passive distension of residual, functioning tissue.

Contractile/noncontractile segment lengths. There are several possible explanations for the observation that the noncontractile segment length decreases with time after a myocardial infarction. The most straightforward is that a peri-infarct rim of noncontractile but perfused tissue (stunned myocardium) regains function in the chronic phase of recovery (18); however, at least two additional possibilities merit consideration. In the dog model, Théroux et al. (19) showed that acute infarction is associated with initial diastolic lengthening and paradoxic motion of the infarct zone. At 4 weeks, when scar formation is complete in the dog, the scar contracts to about 30% of its original diastolic length. The length of the noncontractile segment might be expected to decrease to a comparable degree in patients. Similar results have been reported in echocardiographic (20) and histologic (21) analyses of infarct size during the acute and convalescent phases of myocardial infarction. Additionally, Théroux et al. (19) demonstrated that the compliance of infarcted tissue decreases significantly as a function of time. This decrease in regional compliance may influence the apparent length of the noncontractile segment because of improved tethering and passive inward motion of the scar. The inability to distinguish these mechanisms with angiographic data prevents a precise analysis of the degree to which the present observations represent a reclaiming of function along the rim of the infarction versus scar contraction accompanied by proportionate hypertrophy of the contractile segment.

These findings with regard to the fate of the contractile or noninfarcted segment are in agreement with results of a previous echocardiographic analysis (3) showing significant increase in the length of both infarcted and noninfarcted segments in the late phase after infarction; however, our finding of no further elongation of the noncontractile segment differs from the results of that study. One possible explanation for this discrepancy is that the infarct segment, as defined in the echocardiographic study (all myocardium anterior to the papillary muscles in a short-axis view of the left ventricle), included a substantial component of normal and border zone myocardium. As the present analysis of local curvature and the work of others (22–24) suggest, this border zone myocardium may be at highest stress and therefore is presumably more likely to hypertrophy. Thus, in the echocardiographic study, a substantial component of hypertrophy of viable myocardium within the "infarct segment" may have diluted the effects of change in the true infarct zone. The use of akinesia and dyskinesia may discriminate better between changes in the zone of transmural infarction (25) and those in residual, viable myocardium.

Ventricular geometry. In the normal left ventricle, the apex is the region with the greatest degree of diastolic curvature (shortest radius of curvature), and the curvature increases significantly in this region during systole. As predicted by the law of Laplace, the apical myocardium is also significantly thinner than in regions with a lesser degree

of curvature (26). At 3 weeks after an anterior Q wave infarction we found considerable blunting of the systolic apical curvature peak and an absence of the systolic increase in apical curvature that is important in maintaining normal apical wall stress despite increasing intracavitary pressure during systole. The combination of a highly unfavorable change in local geometry superimposed on the relatively thin myocardium at the apex may help to explain the high incidence of infarct expansion and early aneurysm formation reported with anterior myocardial infarction as opposed to inferior infarction (1,27,28).

Curvature analysis confirms that juxtaposition of viable and akinetic or dyskinetic myocardium after a large anterior myocardial infarction creates a rim of negative or "anticlastic" (26) curvature encircling the infarct during systole, predicting a markedly elevated wall stress for a given wall thickness and pressure and producing the subjective appearance of hyperfunction in the infarct border zone despite normal or depressed quantitative wall motion. Pouleur et al. (24) showed that this peri-infarct zone has high end-systolic and residual (early diastolic) wall stresses in humans, and Anversa et al. (29) demonstrated a reduced oxygenation potential in this critical zone of perfused, viable but hypocontractile myocardium (30). Thus, this zone may be at high risk for further ischemic insult, which may help to explain our observations and those of others (31–33) of impaired contractile performance and islets of necrosis in noninfarcted tissue early after anterior myocardial infarction. This local shape abnormality also may relate to the observation in the rat model of a rim of maximal hypertrophy at the interface between the healing scar and viable myocardium (34). Analysis of regional curvature, a major determinant of wall tension, suggests that this heterogeneous, concentric component of left ventricular hypertrophy after myocardial infarction in the absence of an increased systolic pressure might be attributed to an increase in local wall tension resulting from abnormalities of local curvature, which may undergo significant change independent of ventricular size. Therefore, in the infarcted ventricle, marked abnormalities of local left ventricular geometry, which may occur very early after infarction (35–37), make a regional rather than global analysis of wall stress imperative.

In the year after infarction, global increases in ventricular chamber volume and sphericity are associated with a regional flattening of the high tension rim of hypocontractile anticlastic tissue that surrounds the infarct zone. These changes are accompanied by a decrease in the degree of bulging of the infarcted anterior wall. These changes could be interpreted as a redistribution of regional wall tension as the peri-infarct tissue, including any stunned myocardium, hypertrophies and regains function and the infarcted tissue forms a contracted, less compliant fibrous scar that yields less to high intracavitary pressures (19,22). Histologic scar contraction and stiffening, coupled with lengthening (eccentric hypertrophy) of the contractile myocardial segment, will result in a lesser size and compliance mismatch between functioning and nonfunctioning tissue in systole, leading to a reduction in the degree of local curvature abnormality at the interface between the two. Similarly, regained contractile function at this crucial interface will tend to reduce the local shape abnormality; however, a distinction between regained function improving shape and improved shape augmenting function (because of lower wall stress) becomes difficult to make in this region.

Thus, rather than a cause of increased global wall stress (38), late increases in global sphericity may be viewed as an adaptation to abnormal regional wall stress, with increased sphericity (approaching the spheric value of 2π on curvature plots) affording a redistribution of wall stress away from the critical border zone of viable myocardium. In patients with less severe abnormalities of local shape, this remodeling can occur with no loss of systolic function and, hence, maintenance of a stable systolic volume. However, in patients with infarct expansion and more severe abnormalities of shape, a limit may be reached beyond which these adaptations are inadequate, leading to increased local wall tension, impaired blood flow, further necrosis and deterioration of systolic function with systolic volume enlargement. The latter will provide the stimulus to the eccentric component of hypertrophy and diastolic chamber enlargement.

Effects of therapy. In previous work (10), we have shown that captopril therapy was effective in preventing late volume enlargement in the high risk patient group with persistent occlusion of the infarct-related vessel. In the present analysis, this late volume enlargement in the placebo-treated patients who had an occluded left anterior descending coronary artery was shown to be the result of a change in geometry to a more spheric configuration—a transition that was not present in placebo-treated patients with a patent vessel or in patients with an occluded vessel treated with captopril. Thus, the forces that drive remodeling of the ventricle toward a more spheric configuration (for example, abnormal regional wall stress, hypertrophy of the residual myocardium and contraction of the fibrous scar) were attenuated in patients treated with captopril.

Conclusions. We confirm the occurrence of late ventricular enlargement in a substantial proportion of patients after a large first anterior myocardial infarction. This late chamber enlargement is associated with lengthening of the contractile segment rather than progressive infarct expansion. Further, we have quantitatively assessed the abnormalities in ventricular shape that accompany anterior myocardial infarction and confirm that severe abnormalities of global and regional left ventricular shape are present 3 weeks after infarction and that further changes in geometry contribute significantly to late volume enlargement, suggesting that chamber geometry may play an important role in ventricular remodeling.

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